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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/098,602	03/15/2002	Andrew P. Kloek	12557-004001	7672

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EXAMINER	
SWOPE, SHERIDAN	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 10/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/098,602	KLOEK ET AL.	
	Examiner	Art Unit	
	Sheridan L. Swope	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 July 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response of July 19, 2004 to the First Action on the Merits of this case is acknowledged. It is acknowledged that Claim 4 has been amended, Claims 5-17 have been canceled, and Claim 18 has been added. Claims 1-4 and 18 are hereby examined on their merits.

Claim Rejections - 35 USC § 101

Utility

Rejection of Claims 1-4 under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for the reasons described in the prior action is maintained.

In support of their request that said rejection be withdrawn, Applicants provide the following arguments. (1) That the glutamine-synthetase-like polypeptide of SEQ ID NO: 2 is expected to be useful as a target for the identification of nematicidal compounds because it more closely resembles bacterial glutamine synthetases than mammalian or plant glutamine synthetases and because glutamine synthetases are thought to provide an essential function. (2) That Applicant's assertion that SEQ ID NO: 2 is a GS-like polypeptide is based, in part, on Pfam analysis. Dr. Kloeck explains that the only Pfam domain match above threshold is the glutamine synthetase domain and that SEQ ID NO: 2 has an e-value of $1.7e^{-77}$ with said domain, indicating that the match is unlikely to occur by chance. Further, that Pfam analysis indicates that the glutamine synthetase domain extends from residues 115-375 of SEQ ID NO: 2. (3) Dr. Kloeck's § 1.132 declaration of July 19, 2004 states that a BLAST analysis with SEQ ID NO: 2 reveals that nearly all of the proteins having sequence homology to SEQ ID NO: 2 are identified as

glutamine synthetases. In support of said statement, a list of sequences producing significant alignments is provided (page 3 of the declaration).

These arguments are not found to be persuasive for the following reasons.

(1) As Applicant has stated, a utility for the protein of SEQ ID NO: 2 as a target for identification of nematicidal compounds depends on the identity of said protein as a glutamine synthetase. For the reasons described in the prior action and below, a person of ordinary skill in the art would not conclude that the protein of SEQ ID NO: 2 is a glutamine synthetase.

(2) Applicant's assertion that Pfam analysis demonstrates that the only domain homologous to SEQ ID NO: 2 is a glutamine synthetase domain, with an e-value of $1.7e^{-77}$, is acknowledged. However, the results of Pfam analysis for the protein set forth by SEQ ID NO: 2 would not convince one of skill in the art that said protein is a glutamine synthetase. Pfam analysis merely provides information on the probability of a protein having a domain similar to a domain from a protein of known function; it does not provide conclusive information on whether the query protein has the same function. Furthermore, the e-value for Pfam analysis of SEQ ID NO: 2 is low. As a comparison, the e-value for Pfam analysis of the known glutamine synthetase of Sanangelatoni et al, 1992 (see prior action) with the glutamine synthetase domain model is $9.1e^{-143}$ (EMBL Acc#X60160, see attached analysis). In contrast the e-value for Pfam analysis of SEQ ID NO: 2 with the glutamine synthetase domain model is $1.7e^{-77}$, a difference of e^{-66}! Another known glutamine synthetase (Smart et al, 1998) has a Pfam e-value of $1.5e^{-102}$ with the glutamine synthetase model domain (NCBI Acc#AF004351, see attached analysis). Furthermore, as stated by Dr. Kloeck in his declaration under § 1.132, the alleged glutamine synthetase domain of SEQ ID NO: 2 extends from residues 115-375; there is no disclosure as to

whether residues 1-114 or 376-454 of SEQ ID NO: 2 are consistent with glutamine synthetase activity or any other activity. Based on these data, a person of ordinary skill in the art would conclude that, more likely than not, the protein of SEQ ID NO: 2 has some homology to a domain in glutamine synthetases but would not conclude that the protein of SEQ ID NO: 2 has glutamine synthetase activity.

(3) It is acknowledged that most of the sequences producing significant alignment with SEQ ID NO: 2, as presented in the list on page three of Applicant's declaration, are asserted to be glutamine synthetases. However, none of the proteins on said list have been demonstrated to have glutamine synthetase activity. Furthermore, the only protein on said list to have demonstrated activity is not a glutamine synthetase; the protein set forth by accession numbers gi|15865464|EMBL|CAC81335 is a γ-glutamylisopropylamide synthetase (de Azevedo Wasch et al, 2002; pg 2371, parg 4). In fact, said γ-glutamylisopropylamide synthetase has higher homology with SEQ ID NO: 2 (25.9%) than the known glutamine synthetase having highest homology to SEQ ID NO: 2 (20.2%; Sanangelatoni et al, 1992-see prior action). Thus, a person of ordinary skill in the art would not conclude, based on homology to proteins of known activity, that the protein of SEQ ID NO: 2 is a glutamine synthetase. Furthermore, the specification fails to disclose biochemical evidence that the protein of SEQ ID NO: 2 is a glutamine synthetase.

Therefore, rejection of Claims 1-4 under 35 U.S.C. § 101, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, is maintained. Furthermore, rejection of Claims 1-4 under 35 U.S.C. § 112, first paragraph, because the claimed invention is not supported by either a specific and substantial asserted utility or a

well-established utility and, therefore, one of skill in the art would know how to make and use the invention, is also maintained.

New Claim 18 is rejected under 35 U.S.C. § 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. As described below for the rejection of Claim 18 under 35 U.S.C. § 112, first paragraph, for lack of written description, the specification fails to assert that the polypeptide of SEQ ID NO: 2, or any polypeptide with at least 85% identity with SEQ ID NO: 2, has any amide synthetase activity. Furthermore, the family of amide synthetases is a large and variable family of enzymes with a large number of variable substrates and the potentiality of being involved in many different cellular processes and diseases. Neither specific substrates for the polypeptide of SEQ ID NO: 2, as an amide synthetase, nor specific diseases to be treated with said polypeptide have been identified. Moreover, any use, as stated in the specification, for the polypeptide of SEQ ID NO: 2, or variants thereof, as novel targets for anti-nematode vaccines, pesticides, and drugs (pg 15, lines14-15), to produce immunologically interactive molecules, such as antibodies (pg 32, lines 3-4), or in methods of identifying a compound capable of altering the activity of said polypeptide (pg 34, line 30-31) is either an application that depends on the protein of SEQ ID NO: 2 being a amide synthethase or is an application that would apply to every member of a general class of materials. Thus, the utility is not specific, since all proteins can be used to make antibodies or not substantial, because the use of the protein of SEQ ID NO: 2 as a amide synthetase is only potential and is not in currently available in practical form since, said protein has not been demonstrated to be a amide synthetase.

Double Patenting

Provisional rejection of Claims 1-4 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-4 of copending US application SN10/446,520 is maintained, since Applicants state they will address said rejection when they are notified that the [this] application includes allowable claims.

Claim Rejections - 35 USC § 112-First Paragraph

Enablement

Further rejection of Claims 1-3 under 35 U.S.C. 112, first paragraph because the specification, does not reasonably provide enablement for any polypeptide having at least 85%, 90%, or 95% identity with SEQ ID NO: 2 is maintained. Applicants did not respond to said rejection.

Even if Claim 18 were not rejected under 35 U.S.C. 112, first paragraph because the recited invention lacks utility and, therefore, one skilled in the art clearly would not know how to use the claimed invention, the following rejection would apply.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for any polypeptide having amide synthetase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with this claim, which broadens the scope of the recited invention.

Claim 18 is so broad as to encompass any polypeptide having at least 85% identity with SEQ ID NO 2 and having amide synthetase activity. The scope of this claim is not commensurate with the enablement provided by the disclosure with regard to the extremely large

number of polypeptides broadly encompassed by the claim. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired amide synthetase activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. In the instant application polypeptides having any amide synthetase activity have not been disclosed.

While recombinant and mutagenesis techniques as well as assays for testing various amide synthetase activities are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the results of such modifications are unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Furthermore, other than for glutamine synthetase, the specification fails to provide any guidance as to the specific assays to be used to measure the activity of any other specific amide synthetase, which is a large family of enzymes.

The specification does not support the broad scope of Claim 18 which, encompasses all polypeptides having at least 85% identity with SEQ ID NO: 2 and having any amide synthetase activity. The specification does not support the broad scope of Claim 18 because the specification does not establish: (A) the specific amide synthetase activities recited; (B) the

specific assays to measure each specific amide synthetase activity; (C) regions of the protein structure which may be modified without effecting any specific amide synthetase activity; (D) the general tolerance of any specific amide synthetase activity to modification and extent of such tolerance; (E) a rational and predictable scheme for modifying any residues with an expectation of obtaining the desired specific amide synthetase activity; and (F) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of polypeptides having amide synthetase activity with an enormous number of amino acid modifications of the polypeptide of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of the identity of sequences having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Rejection of Claims 1-3 under 35 U.S.C. 112, first paragraph, for insufficient written description, as described in the prior action, is maintained. In support of their request that said rejection be withdrawn, Applicants argue that the presently claimed nucleic acid molecules are defined by sequence or by sequence combined with function. These arguments are not found to be persuasive because (1) the invention being examined recites polypeptides, not

polynucleotides; (2) claims 1-3 recite sequence but no function and the specification fails to describe the function of all polypeptide having at least 85%, 90%, or 95% homology with SEQ ID NO: 2.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Although glutamine synthetase is an amide synthetase, recitation of polypeptides having any amide synthetase activity is not disclosed in the specification. Therefore, said recitation in Claim 18 is considered to be New Matter.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan L. Swope whose telephone number is 703-305-1696 (571-272-0943 after January 12, 2004). The examiner can normally be reached on M-F; 9:30-7 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Sheridan Lee Swope, Ph.D.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600